Meroterpenoid Synthesis via Sequential Polyketide Aromatization and Cationic Polyene Cyclization: Total Syntheses of (+)-Hongoquercin A and B and Related Meroterpenoids

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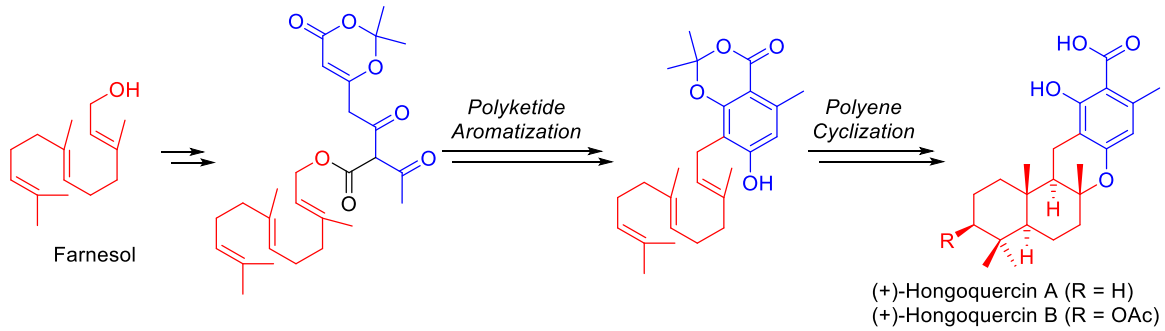
ABSTRACT GRAPHIC



ABSTRACT

(+)-Hongoquercin A and B were synthesized from commercially available *trans,trans*-farnesol in 6- and 11-steps respectively using dual biomimetic strategies with polyketide aromatization and subsequent polyene functionalization from a common farnesyl-resorcylate intermediate. Key steps involve Pd(0)-catalyzed decarboxylative allylic rearrangement of a dioxinone β,δ-diketo-ester to a β,δ-diketo-dioxinone, which was readily aromatized into the corresponding resorcylate, and subsequent polyene cyclization via enantioselective protonation or regioselective terminal alkene oxidation and cationic cyclization of enantiomerically enriched epoxide to furnish the tetracyclic natural product cores. Analogs of the hongoquercin were synthesized via halonium-induced polyene cyclizations, and the meroterpenoid could be further functionalized via saponification, hydrolytic decarboxylation, reduction and amidation reactions.

INTRODUCTION

(+)-Hongoquercin A (**1**) and B (**2**) were isolated from the fermentation broths produced by an unidentified fungus in 1998 independently by Roll and Abbanat (**Figure 1**).[1] They exhibited modest antibacterial activity against methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus faecium*.[1] These natural products are meroterpenoids which have a mixed biosynthetic origin involving polyketide and terpenoid pathways. (-)-Siccanin (**3**) and (-)-austalide K (**4**) are additional examples of such structurally diverse bioactive meroterpenoids.[2]

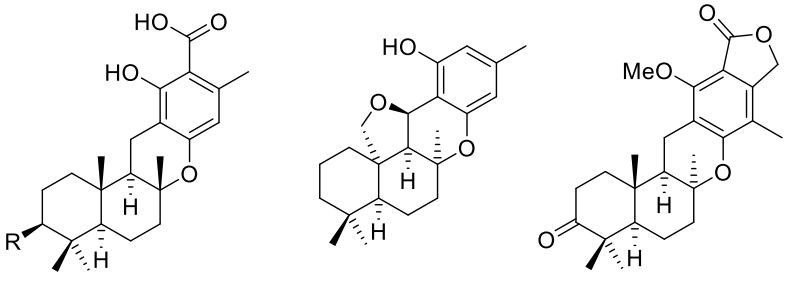
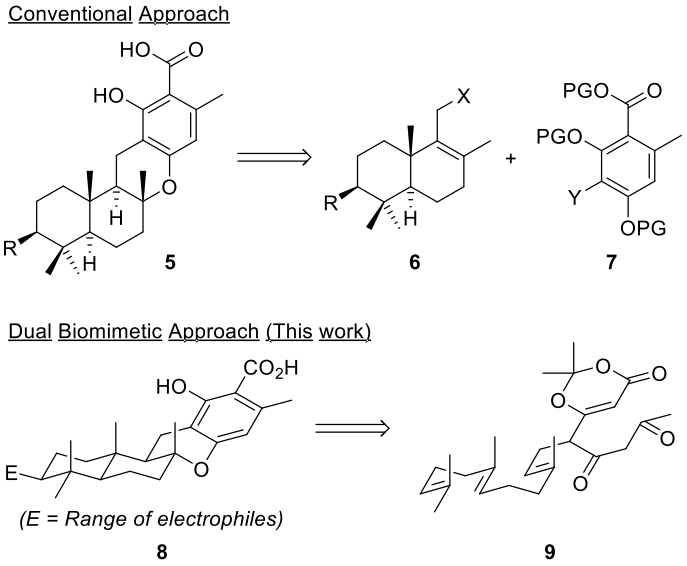


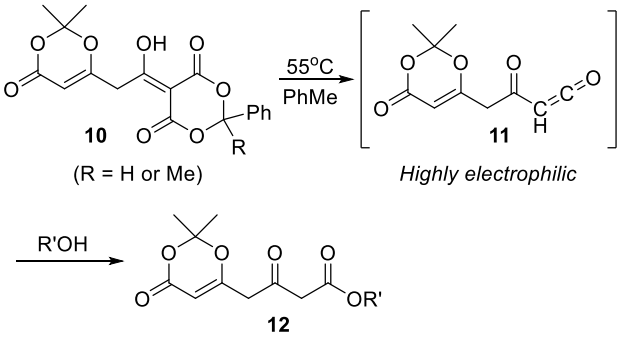
Figure 1. Bioactive meroterpenoid natural products.

Over the last two decades, several total syntheses of hongoquercins **5** have been reported.[3] The common synthetic strategy involves the coupling of two synthons, an enantiopure synthesized drimene **6** coupled with a substituted resorcinol derivative **7** (**Scheme 1**). However, this conventional approach often requires extensive use of protecting groups on the resorcinol unit **7** and multistep transformations for the synthesis of the precursor drimene **6**. Most of the reported processes for the preparation of the resorcinol rely on extensive derivatization of an aromatic precursor while alternative synthetic strategies to prepare resorcinol, such as benzannulation, have been shown to be more concise and flexible.[4] Therefore, we considered that a dual biomimetic approach for elaborating the arene ring and tricyclic terpenoid residues from acyclic precursor **9** sequentially via cascade cyclizations would simplify the syntheses of these natural products. Additionally, if the farnesyl residue was functionalized after aromatization to construct the resorcylate entity, a diverse range of hongoquercin analogs **8** should be available by variation of the electrophilic reagents used in such derivatizations.



Scheme 1. Synthetic strategies of the hongoquercins **5**.

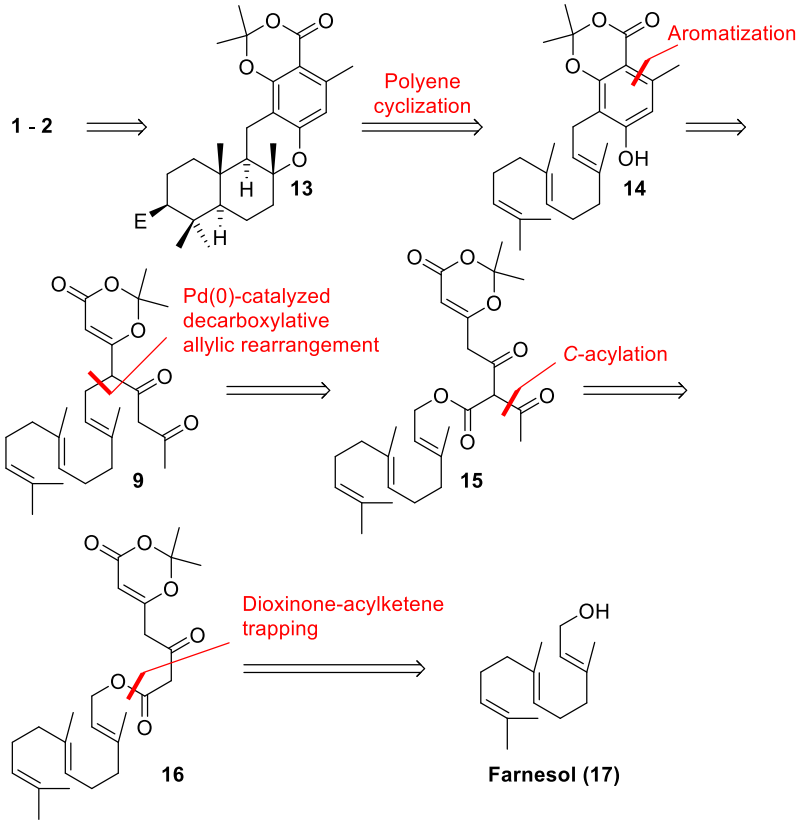
Inspired by the pioneering work of the Harris group and Hyatt group respectively on the biomimetic synthesis of β-resorylate and on the generation of acyl-ketenes by the thermolysis of dioxinones,[5,6] our group has developed a biomimetic route to β-resorylate natural products that utilizes β,δ-diketo-dioxinones as masked triketo-ketenes.[7] In 2009, we additionally discovered a regioselective palladium(0)-catalyzed decarboxylative rearrangement during the synthesis of aigialomycin D.[8] Application of this reaction greatly facilitated the synthesis of meroterpenoid resorcylate natural products.[9] More recently, we developed an efficient methodology for the synthesis of dioxinone β-keto esters **12** using dioxane-4,6-dione-keto dioxanones **10** as the masked dioxinone-acyl-ketene **11** (**Scheme 2**).[10] Application of this reaction provided an efficient route for the synthesis of β-resorylates and its utility has been showcased in the total syntheses of several bioactive meroterpenoid natural products.[10] Herein we report further extensive studies on the dual biomimetic total synthesis of the hongoquercins **5**, which we initially published as a communication.[9e]



Scheme 2. Thermolysis of dioxane-4,6-dione-keto dioxanones **10**.

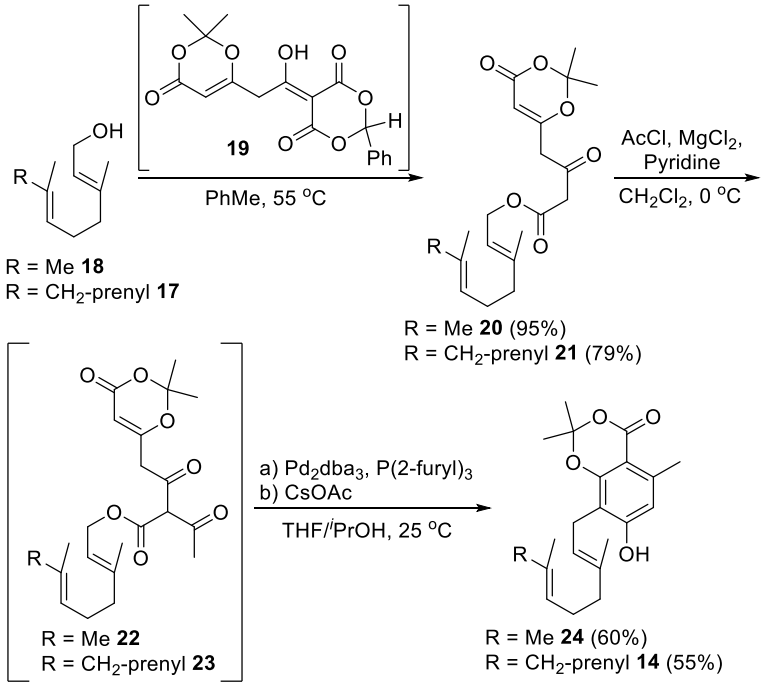
RESULTS AND DISCUSSION

We considered that the key meroterpenoids **13** should be available using a polyene cyclization from resorcylate **14** by enantioselective electrophilic reactions with chiral Brønsted acids (E = H), epoxidation and subsequent reaction with a Lewis acid (E = OH) or halogenations with reagents that provide halonium ion intermediates (E = Br and I) (**Scheme 3**). The common resorcylate intermediate **14** should be available from the cycloaromatization of *β,δ*-diketo-dioxinone **9**, which could be synthesized via palladium(0)-catalyzed decarboxylative allylic rearrangement of dioxinone *β,δ*-diketo-ester **15**. Dioxinone *β,δ*-diketo-ester **15** in turn should be available via *C*-acylation of dioxinone *β*-keto-ester **16**, which in turn is available from trapping a dioxinone-acylketene with *trans,trans*-farnesol (**17**).[10]



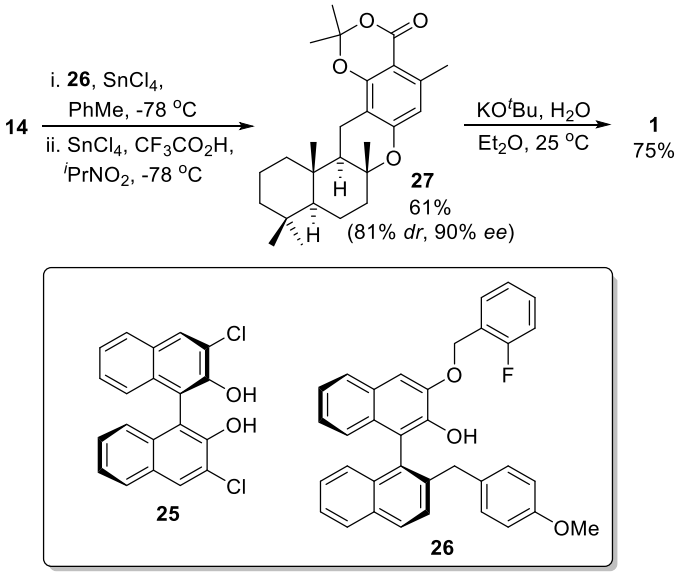
Scheme 3. Retrosynthetic analyses of hongoquercins A (**1**) and B (**2**).

Following our recently published methods,[10] thermolysis of dioxane-4,6-dione-keto dioxanone **19** at 55 °C generated the dioxinone acyl-ketene **11**, which was trapped with *trans,trans*-farnesol (**17**) to provide dioxinone *β*-keto-ester **21** (79%) (**Scheme 4**). Magnesium chloride mediated regioselective *C*-acylation of *β*-keto-ester **21** with acetyl chloride gave dioxinone *β,δ*-diketo-ester **23**, which on reaction with $Pd_2(dba)_3$ and tri(2-furyl)phosphine resulted in a highly regioselective decarboxylative allylic rearrangement giving the *β,δ*-diketo dioxinone **9** and readily aromatized *in situ* to produce farnesyl resorcylate **14** (55% overall from **21**). A geranyl substituted analog **24** was also synthesized, using the same reaction sequence, from geraniol (**18**) in 3 steps with an overall yield of 57%.



Scheme 4. Synthesis of the terpene resorcylates **14** and **24**.

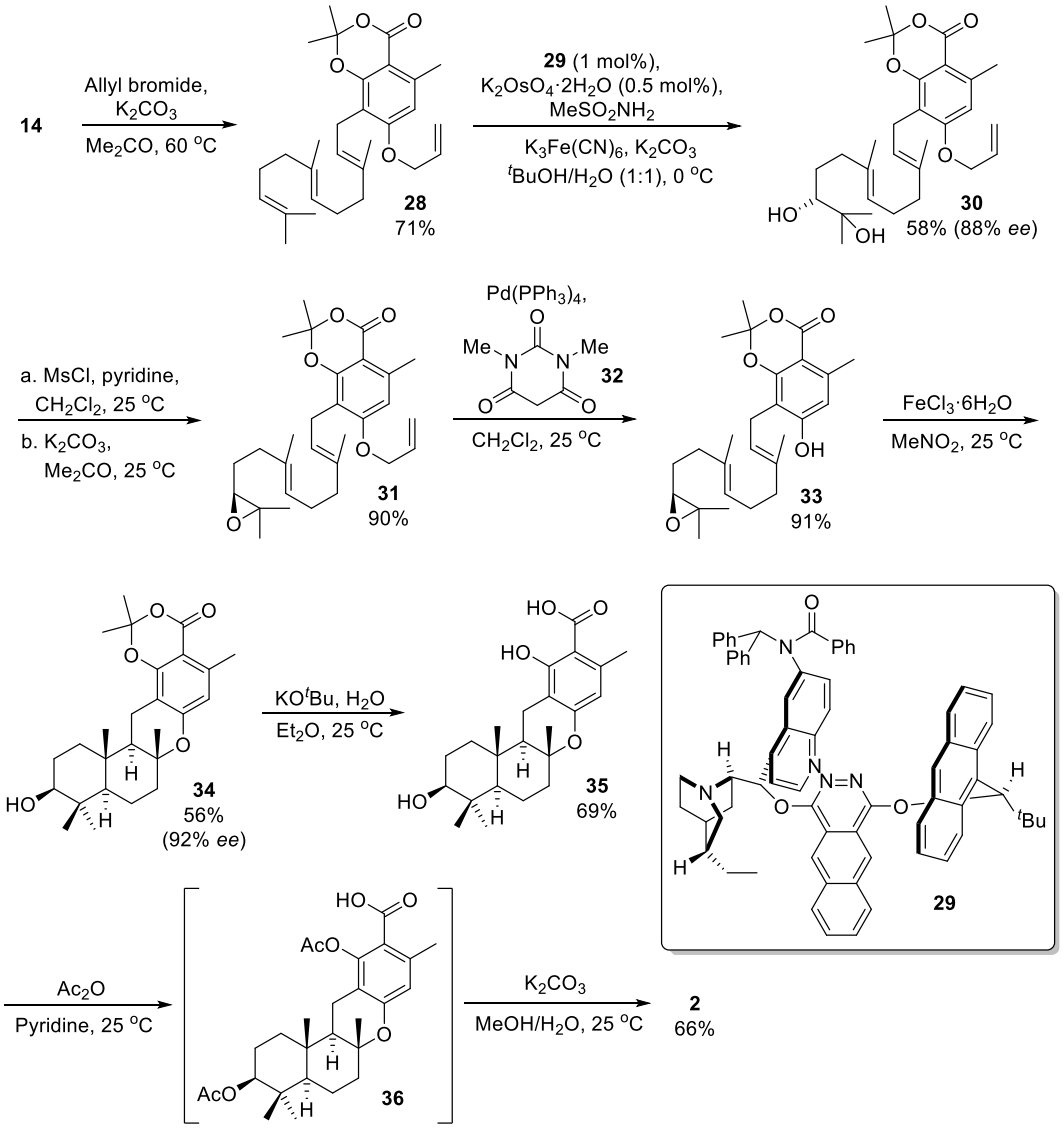
We first investigated the synthesis of (+)-hongoquercin A (**1**) via enantioselective protonation of farnesyl resorcylate **14** (**Scheme 5**) using the Lewis acid enhanced chiral Brønsted acids derived from antimony pentachloride with binol **25** and stannic chloride with binol **26** as introduced by Corey *et al*[11] and Yamamoto *et al*.[12] Enantioselective protonation with $SbCl_5$·**25** gave a mixture of partially cyclized products from which the desired meroterpenoid **23** was isolated in 15% yield and with an enantiomeric excess of 20% as determined by chiral HPLC. Fortunately, the cyclization using $SnCl_4$·**26** as the dual Brønsted and Lewis acids was highly enantioselective and gave the desired meroterpenoid **27** (61%, 81% *dr* and 90% *ee* as determined by chiral HPLC) on sequential reaction with $SnCl_4$·**26** and $SnCl_4$ and trifluoroacetic acid. Finally, saponification[13] of meroterpenoid **27** gave (+)-hongoquercin A (**1**) (75%) with an overall yield of 20% over 5 steps from *trans*,*trans*-farnesol **17**. The spectroscopic data were in full agreement with that reported for the isolated natural product[1] and the structure was unambiguously confirmed by a single X-ray crystallography.



Scheme 5. Total synthesis of (+)-hongoquercin A (**1**).

Next, we focused on the synthesis of (+)-hongoquercin B which utilized enantioselective epoxidation (**Scheme 6**). Whilst we had reported the synthesis of this natural product from the farnesyl derivative **33**,[9e] we wished to reinvestigate this synthesis with late-stage oxidation of the terminal alkene on the pendant farnesyl side chain since this should greatly facilitate the synthesis and bioassay of a focused library of novel

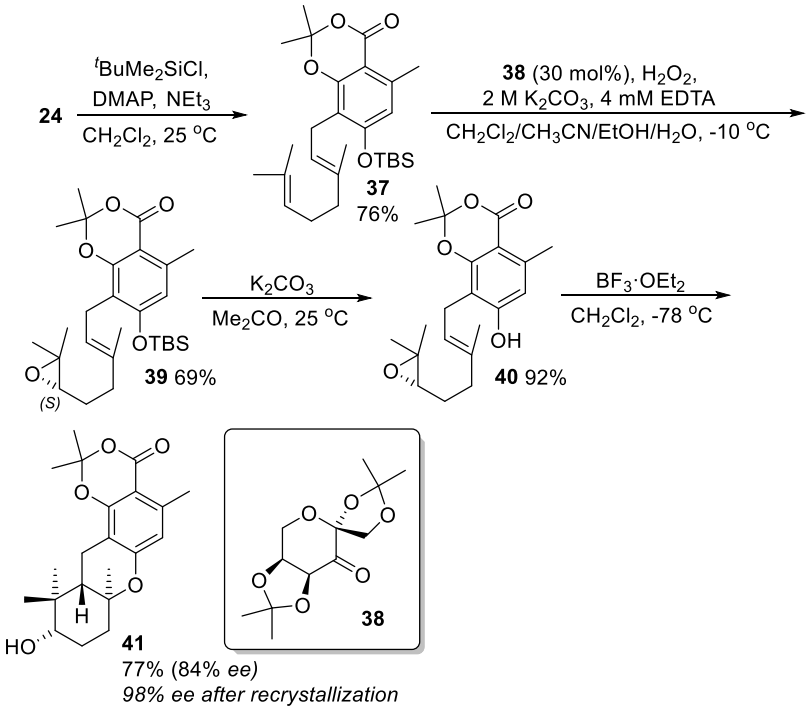
hongoquercin analogs with the late stage introduction of terpene structural diversity. In order to effect such electrophilic functionalization of the terminal alkene unit, we needed to suppress phenol-directed oxidation.[14] We found that protection by phenol allylation suitable for this purpose. Allylation of farnesyl resorcylate **14** gave allyl ether **28** (77%), which was subjected to dihydroxylation in the presence of the Corey dihydroquinidine ligand **29** thereby producing the (*R*)-diol **30** (58%, 78% brsm, 88% *ee* as determined by Mosher ester analysis).[15] Diol **30** was subsequently converted into the (*S*)-epoxide **31** (93%) via mesylation and potassium carbonate mediated cyclization. The allyl protecting group was selectively removed by reaction with dimethylbarbituric acid **32** catalyzed by $Pd(PPh_3)_4$ to provide epoxide **33** (91%).[16] After screening a variety of different Lewis acids with epoxide **33**, it was found that ferric chloride hydrate was a superior Lewis acid catalyst to boron trifluoride etherate,[9e] which we previously reported for this cyclization of epoxide **33** to provide meroterpenoid **34.** The use of boron trifluoride etherate often led to the formation of undesired by-products such as bicyclic ethers and partially cyclized products. Such side reactions and irreproducibility were substantially suppressed using ferric chloride hydrate.[17] Thus, treatment of epoxide **33** with $FeCl_3 \cdot 6H_2O$ resulted in biomimetic cationic cyclization to give meroterpeonoid **34** (56%, 92% *ee* as determined by chiral HPLC) as a single diastereoisomer. Saponification of meroterpenoid **34** gave acid **35** (69%),[13] which was subjected to acetylation to provide diacetate **36**. Subsequent selective deacetylation of the phenolic acetate gave (+)-hongoquercin B (66%) with an overall yield of 3.7% over 11 steps. The analytical data for this synthetic material are in full agreement with that reported for the isolated natural product.[1]



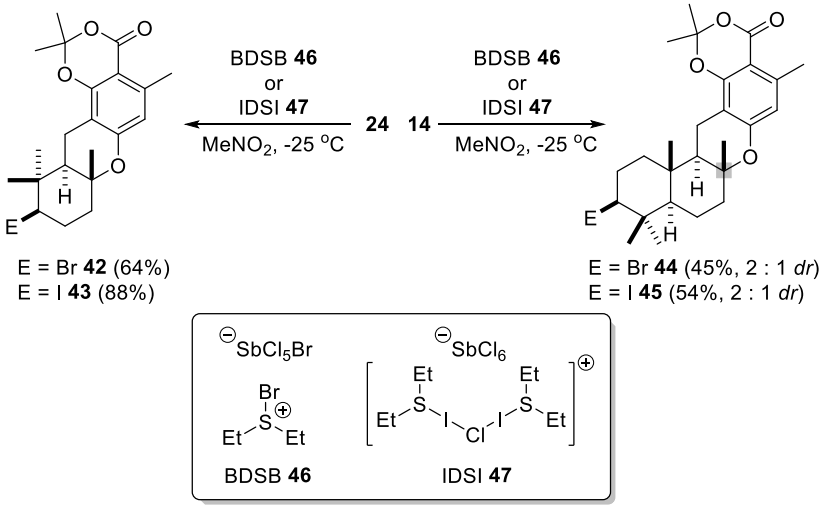
Scheme 6. Total synthesis of (+)-hongoquercin B (**2**).

Additional meroterpenoids analogs were prepared via epoxidation (**Scheme 7**) and halogenations (**Scheme 8**). Firstly, the geranyl-substituted resorcylate **24** was protected as its silyl ether **37** (76%) and epoxidized with

the dioxirane derived from the Shi chiral ketone **38** to give epoxide **39** (69%).[18] Subsequent deprotection gave epoxide **40** (92%), which was cyclized using boron trifluoride etherate to give meroterpenoid **41** (77%, 84% *ee* as determined by chiral HPLC) as a single diastereoisomer. The (*S*)-enantiomer of meroterpenoid **41** (98% *ee* as determined by chiral HPLC) was obtained by recrystallization to enhance chiral purity. Secondly, we examined the halonium-induced polyene cyclization of the resorcylates to produce additional analogs (**Scheme 8**).[19] Reaction of the geranyl resorcylate **24** with the Snyder reagents $Et_2SBr{\cdot}SbCl_5Br$ (BDSB, **46**) and $(Et_2SI)_2Cl{\cdot}SbCl_6$ (IDSI, **47**) resulted in bromo- and iodo-cyclizations to produce the racemic bromo-meroterpenoid **42** (64%) and racemic iodo-meroterpenoid **43** (88%) as single diastereoisomer, respectively. Racemic bromide **44** (45%, 2 : 1 *dr*) and racemic iodide **45** (54%, 2 : 1 *dr*) were also successfully synthesized from farnesyl-substituted resorcylate **14** using the BDSB **46** and IDSI **47** mediated halocyclizations.[20]



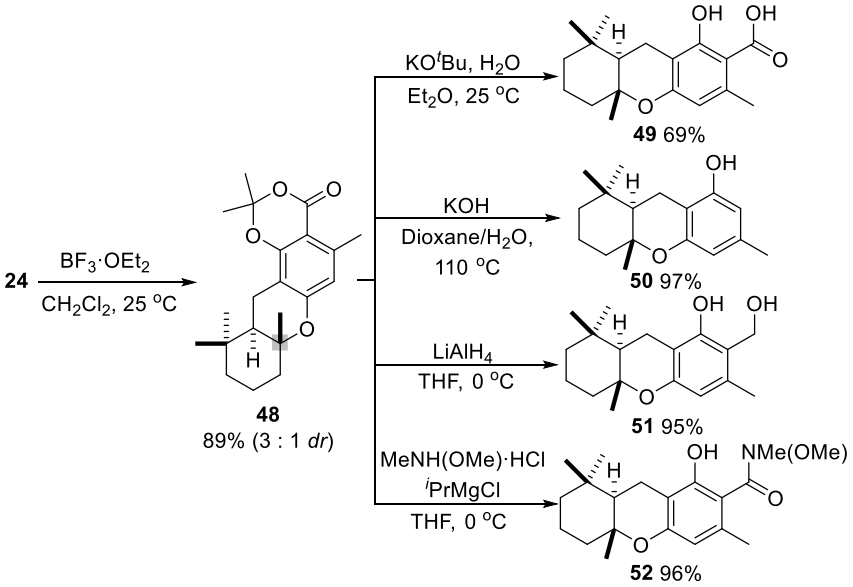
Scheme 7. Synthesis of meroterpenoid **41**.



Scheme 8. Halocyclizations to produce meroterpenoids **42** – **45**.[20]

The 2,2-dimethyl-1,3-benzodioxan-4-one moiety of the meroterpenoids intermediates was also used in alternative derivatization reactions (**Scheme 9**). Thus, reaction of the geranyl-substituted resorcylate **24** with boron trifluoride etherate at 25 °C gave the racemic meroterpenoid **48** (89%, 3 : 1 *dr*) and the desired pure *trans*-fused ring product was obtained by recrystallization from *n*-hexane.[21] Saponification[13] of meroterpenoid **48** gave racemic carboxylic acid **49** (69%) while hydrolytic decarboxylation gave racemic phenol **50** (97%).

Furthermore, reduction of meroterpenoid **48** with $LiAlH_4$ gave racemic diol **51** (95%) and racemic Weinreb amide **52** (96%) was obtained following Grignard reagent mediated amidation.[22]



Scheme 9. Synthesis and functionalizations of meroterpenoid **48**.

CONCLUSION

In conclusion, the total synthesis of (+)-hongoquercin A (**1**) and B (**2**) were completed in 5- and 11-steps, respectively with an overall yield of 20% and 3.7% via a dual biomimetic approach involving sequential polyketide and late stage electrophile mediated polyene cyclizations. Several analogs were synthesized by epoxidation or bromo- and iodo-cyclizations. The meroterpenoids were additionally functionalized using saponification, hydrolytic decarboxylation, reduction and Grignard reagent mediated amidation reactions. Further studies on the synthesis of novel meroterpenoids adopting such dual biomimetic approach are ongoing in our laboratory.

EXPERIMENTAL SECTION

General methods. All reagents and solvents were used directly without further purification unless otherwise stated. The preparation of malonate and dioxinone acid were according to Barrett *et al.*[10b] Binol **25** and binol **26** were prepared respectively according to the procedures reported by Corey *et al.*[11] and Yamamoto *et al.*[12] Dihydroquinidine ligand **29** was prepared according to Corey *et al.*[15] $Et_2SBr{\cdot}SbCl_5Br$ (BDSB, **46**) and $(Et_2SI)_2Cl{\cdot}SbCl_6$ (IDSI, **47**) were prepared according to the method published by Synder *et al.*[19] All solvents were purified and dried by distillation under an atmosphere of N_2 before use. The chiral ketone **38** was prepared from *L*-fructose according to the established method by Shi *et al.*[18] Et_2O and THF were redistilled from Na-Ph_2CO. CH_2Cl_2, Et_3N, MeOH, $^iPrNO_2$ and $MeNO_2$ and pyridine were redistilled from CaH_2 and PhMe was redistilled from Na. All air- and moisture-sensitive reactions were carried out under an atmosphere of N_2 using standard Schlenk techniques in oven-dried glassware equipped with a magnetic stirring bar. The progress of reactions was monitored by analytical thin layer chromatography (TLC) on silica gel coated aluminum oxide F_{254} plates. Developed TLC were visualized under UV light and stained with acidic vanillin solution. Flash column chromatography was performed employing silica gel 60 Å, particle size 40 - 63 μm. The enantiomeric excesses of the compounds were determined by chiral HPLC analysis on Chiralpak® IE column with *n*-hexane and ^{i}PrOH as the mobile phase. All ^1H and ^{13}C NMR spectra were recorded at 400 MHz and 101 MHz respectively at ambient temperature in deuterated solvent as noted. NMR spectra were referenced to residual solvent peaks ($CDCl_3$: $\delta = 7.26$ for ^1H NMR and $\delta = 77.0$ for ^{13}C NMR; CD_3OD $\delta = 3.31$ & 4.87 for ^1H NMR and $\delta = 49.0$ for ^{13}C NMR; $(CD_3)_2CO$: $\delta = 2.05$ for ^1H NMR and $\delta = 29.8$ for ^{13}C NMR) and chemical shifts were reported in ppm. IR spectra are reported in cm^{-1}. Optical rotations were recorded with a polarimeter with the specified concentration and temperature. Mass spectra were obtained

from the Imperial College Mass Spectrometry Service. Melting points were uncorrected. X-ray diffraction data were recorded by the Imperial College X-ray Crystallography Facility.

General procedures for the synthesis of dioxinone *β*-keto esters. 2-Phenyl-1,3-dioxane-4,6-dione (6.91 g, 36.0 mmol), DCC (7.43 g, 36.0 mmol) and DMAP (4.40 g, 36.0 mmol) were dissolved in CH_2Cl_2 (300 mL) and the resulting mixture was stirred for 5 min at 25 °C. 2-(2,2-Dimethyl-4-oxo-4*H*-1,3-dioxin-6-yl)acetic acid (6.70 g, 36.0 mmol) was added with stirring at 25 °C. After 18 h, the mixture was cooled to 0 °C and the insoluble solid was filtered off and washed with CH_2Cl_2 (15 mL). The filtrate was washed with aqueous HCl (1 M; 2 × 200 mL) and the two phases were separated and the organic layer was dried $MgSO_4$), filtered, and concentrated under reduced pressure to give the crude delicate dioxane-4,6-dione-keto-dioxinone **19** as yellow foam, which was used directly without further purification. Crude dioxane-4,6-dione-keto-dioxinone **19** and geraniol (**18**) or *trans*,*trans*-farnesol (**17**) (20.0 mmol) were dissolved in PhMe (150 mL) and stirred at 55 °C for 4 h. The reaction mixture was concentrated under reduced pressure and the brown residue chromatographed (pentane : EtOAc 9 : 1 to 4 : 1) to provide the dioxinone *β*-keto esters **20** and **21** respectively.

(*E*)-3,7-Dimethylocta-2,6-dienyl 4-(2,2-dimethyl-4-oxo-4*H*-1,3-dioxin-6-yl)-3-oxobutanoate (20). Dioxinone *β*-keto-ester **20** (6.92 g, 19.0 mmol, 95%), prepared from geraniol (**18**) (3.47 mL, 20.0 mmol), was obtained as a pale yellow oil: R_f 0.20 (pentane : EtOAc 4 : 1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.36 (s, 1H), 5.34 – 5.30 (m, 1H), 5.09 – 5.04 (m, 1H), 4.67 (d, *J* = 7.2 Hz, 2H), 3.51 (s, 2H), 3.50 (s, 2H), 2.14 – 2.01 (m, 4H), 1.71 (s, 6H), 1.68 (s, 3H), 1.67 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.6, 166.3, 163.5, 160.4, 143.6, 132.0, 123.5, 117.3, 107.3, 97.1, 62.6, 49.1, 46.9, 39.5, 26.2, 25.6, 25.0, 17.7, 16.5; IR ν_{max} (neat) 1720, 1375, 1272, 1201, 1015 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{29}O_6$ 365.1964; Found 365.1977.

(2*E*,6*E*)-3,7,11-Trimethyldodeca-2,6,10-trienyl 4-(2,2-dimethyl-4-oxo-4*H*-1,3-dioxin-6-yl)-3-oxobutanoate (21). Dioxinone *β*-keto-ester **21** (6.81 g, 15.7 mmol, 79%), prepared from *trans*,*trans*-farnesol (**17**) (5.02 mL, 20.0 mmol), was obtained as a pale yellow oil: R_f 0.36 (pentane : Et_2O 1 : 1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (s, 1H), 5.33 – 5.28 (m, 1H), 5.11 – 5.02 (m, 2H), 4.65 (d, *J* = 7.2 Hz, 2H), 3.49 (s, 2H), 3.48 (s, 2H), 2.13 – 1.99 (m, 6H), 1.99 – 1.91 (m, 2H), 1.69 (s, 6H), 1.66 (s, 3H), 1.65 (s, 3H), 1.57 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.6, 166.3, 163.5, 160.4, 143.5, 135.5, 131.2, 124.2, 123.4, 117.3, 107.2, 97.0, 62.5, 49.0, 46.9, 39.6, 39.4, 26.6, 26.1, 25.6, 24.9, 17.6, 16.4, 15.9; IR ν_{max} (neat) 2922, 1722, 1639, 1375, 1272, 1202, 1015, 901, 806 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{25}H_{37}O_6$ 433.2590; Found 433.2598; Anal. Calcd for $C_{25}H_{36}O_6$: C, 69.42; H, 8.39; Found: C, 69.49; H, 8.24.

General procedure for the synthesis of resorcylates 14 and 24. $MgCl_2$ (476 mg, 5.00 mmol) and pyridine (0.810 mL, 10.0 mmol) were added with stirring to *β*-keto-ester **20** or **21** (5.00 mmol) in CH_2Cl_2 (25 mL) at 0 °C. After 15 min, AcCl (0.540 mL, 7.50 mmol) was added dropwise and the reaction mixture was further stirred for 1 h at 0 °C. Reaction was quenched by addition of saturated aqueous NH_4Cl (20 mL) and the pH was adjusted to ~ 2 with aqueous HCl (1 M). The two phases were separated and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give the crude dioxinone *β*,*δ*-diketo-ester **22** or **23**. P(2-furyl)$_3$ (232 mg, 1.00 mmol) and Pd_2dba_3 (229 mg, 0.250 mmol) were added sequentially with stirring to this crude material in THF (30 mL) at 25 °C. After 1 h, CsOAc (2.88 g, 15.0 mmol) in ^{i}PrOH (30 mL) was added and the resulting mixture was stirred for additional 1.5 h. Reaction was quenched with aqueous HCl (1 M; 30 mL) and the two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated under reduced pressure and chromatographed (pentane : EtOAc 19 : 1 to 10 : 1) to give resorcylate **24** or **14**.

(*E*)-8-(3,7-Dimethylocta-2,6-dienyl)-7-hydroxy-2,2,5-trimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (24). Resorcylate **24** (1.03 g, 3.02 mmol, 60% over 2 steps), prepared from dioxinone *β*-keto-ester **20** (1.83 g, 5.00 mmol), was obtained as a white solid. An analytically pure sample was obtained by recrystallisation from $MeNO_2$: R_f 0.37 (pentane : EtOAc 4 : 1); m.p. 102.9 – 103.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.42 (s, 1H), 6.06 (s, 1H), 5.19 (t, *J* = 7.4 Hz, 1H), 5.04 (t, *J* = 6.3 Hz, 1H), 3.33 (d, *J* = 7.2 Hz, 2H), 2.59 (s, 3H), 2.14 – 1.98 (m, 4H), 1.79 (s, 3H), 1.69 (s, 6H), 1.67 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.2,

160.2, 156.0, 142.8, 138.5, 132.0, 123.7, 120.8, 113.7, 112.8, 105.3, 104.8, 39.7, 26.4, 25.7, 25.6, 22.0, 21.9, 17.7, 16.2; IR ν_{max} (neat) 3199, 1694, 1608, 1300, 1282, 1210, 1177, 1106, 1045, 754 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{21}H_{29}O_4$ 345.2066; Found 345.2067; Anal. Calcd for $C_{21}H_{28}O_4$: C, 73.32; H, 8.19; Found: C, 73.35; H, 8.31.

7-Hydroxy-2,2,5-trimethyl-8-((2*E*,6*E*)-3,7,11-trimethyldodeca-2,6,10-trienyl)-4*H*-benzo[*d*][1,3]dioxin-4-one (14). Resorcylate **14** (1.14 g, 2.75 mmol, 55% over 2 steps), prepared from dioxinone *β*-keto-ester **21** (2.17 g, 5.00 mmol), was obtained as a yellow oil, which solidified upon standing: R_f 0.24 (pentane : EtOAc 9 : 1); m.p. 72.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.41 (s, 1H), 6.15 (s, 1H), 5.19 (t, *J* = 6.7 Hz, 1H), 5.13 – 5.00 (m, 2H), 3.32 (d, *J* = 7.2 Hz), 2.58 (s, 3H), 2.14 – 1.90 (m, 8H), 1.79 (s, 3H), 1.68 (s, 6H), 1.67 (s, 3H), 1.58 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 160.0, 156.0, 142.8, 138.6, 135.6, 131.3, 124.3, 123.5, 120.8, 113.6, 112.7, 105.3, 104.8, 39.7, 39.7, 26.7, 26.3, 25.7, 25.7, 22.0, 21.9, 17.7, 16.2, 16.0; IR ν_{max} (neat) 3209, 2971, 2926, 1738, 1704, 1964, 1606, 1590, 1376, 1284, 1217, 1170, 1107, 1046, 858, 751 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{26}H_{37}O_4$ 413.2692; Found 413.2680; Anal. Calcd for $C_{26}H_{36}O_4$: C, 75.69; H, 8.80; Found: C, 75.56; H, 8.96.

(7a*R*,9a*S*,*13aS*,13b*R*)-2,2,5,7a,10,10,13a-Heptamethyl-7a,8,9a,10,11,12,13,13a,13b,14-decahydro-4*H*,9*H*-benzo[*a*][1,3]dioxino[5,4-*j*]xanthen-4-one (27). $SnCl_4$ in heptane (1 M; 0.750 mL, 0.750 mmol) was added with stirring to binol **26** (463 mg, 0.900 mmol) in PhMe (9 mL) at 25 °C. After 10 min, the mixture was cooled to -78 °C, when resorcylate **14** (124 mg, 0.300 mmol) in PhMe (1.5 mL) was added dropwise and the reaction mixture was further stirred for 48 h at -78 °C. Reaction was quenched with $NaHCO_3$ (15 mL) and the mixture diluted with Et_2O (10 mL). The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (4 × 15 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : Et_2O 9 : 1 to PhMe : Et_2O 12 : 1) to recover the binol **26**. The crude mixture of products was then dissolved in 2-nitropropane (6 mL) and cooled to -78 °C. $SnCl_4$ in heptane (1 M; 0.750 mL, 0.750 mmol) and CF_3COOH (0.230 mL, 3.00 mmol) were sequentially added dropwise with stirring at -78 °C. After 24 h, reaction was quenched with saturated aqueous $NaHCO_3$ (10 mL) and diluted with Et_2O (10 mL). The two phases were separated, and the aqueous layer was extracted with Et_2O (4 × 15 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : Et_2O 9 : 1) to provide meroterpenoid **27** (78 mg, 0.189 mmol, 63%, 80% *dr*, 90% *ee*, measured by chiral HPLC, Chiralpak® IE column, *n*-hexane : ^{i}PrOH 19 : 1, 5 mL/min, t_R = 15.9 [(+)-enantiomer], 14.9 [(-)-enantiomer] min) as a colorless oil containing a mixture of diastereoisomers. An analytical sample was purified by preparative chiral HPLC: R_f 0.75 (pentane : EtOAc 9 : 1); $[\alpha]_D^{20}$ + 80.3° (*c* 0.57, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.33 (s, 1H), 2.57 (s, 3H), 2.53 (dd, 1H), 2.24 (dd, *J* = 16.8, 13.2 Hz, 1H), 2.08 (dt, *J* = 12.5, 3.2 Hz, 1H), 1.82 – 1.77 (m, 1H), 1.77 – 1.74 (m, 1H), 1.72 (s, 3H), 1.69 (s, 3H), 1.68 – 1.65 (m, 1H), 1.65 – 1.62 (m, 1H), 1.53 (d, *J* = 5.3 Hz, 1H), 1.52 – 1.45 (m, 1H), 1.45 – 1.39 (m, 1H), 1.39 – 1.34 (m, 1H), 1.19 (s, 3H), 1.16 (dd, *J* = 13.5, 4.3 Hz, 1H), 1.02 (dd, *J* = 12.2, 2.3 Hz, 1H), 0.98 (dd, *J* = 12.8, 3.8 Hz, 1H), 0.91 (s, 6H), 0.85 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.9, 158.7, 156.1, 142.0, 114.3, 108.3, 104.8, 103.9, 78.4, 56.1, 51.3, 41.8, 40.8, 39.2, 36.9, 33.4, 33.2, 26.2, 25.5, 22.0, 21.6, 20.7, 19.7, 18.5, 16.5, 14.9; IR ν_{max} (neat) 2928, 2867, 1728, 1616, 1575, 1452, 1388, 1285, 1127 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{26}H_{37}O_4$ 413.2696; Found 413.2698.

(+)-Hongoquercin A [(4a*S*,6a*R*,12a*R*,12b*S*)-11-Hydroxy-4,4,6a,9,12b-pentamethyl-1,3,4,4a,5,6,6a,12,12a,12b-decahydro-2*H*-benzo[*a*]xanthene-10-carboxylic acid (1)] H_2O (7 *μ*L, 0.383 mmol) was added with stirring to a suspension of meroterpenoid **27** (79.0 mg, 0.191 mmol) and KO^{t}Bu (172 mg, 1.53 mmol) in Et_2O (3 mL) at 25 °C. After 2 h, ice was added until two layers were formed and the two phases were separated. The organic layer was extracted with H_2O (5 × 5 mL) and the combined aqueous layers were acidified with HCl (4 M) to pH ~ 1. The two phases were separated and the aqueous layer was extracted with Et_2O (5 × 5 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : EtOAc : AcOH 9 : 1 : 0.01) to afford (+)-hongoquercin A (**1**) (53 mg, 0.142 mmol, 75%) as white solid. An analytical sample was prepared by recrystallization (pentane : CH_2Cl_2): R_f 0.25 (pentane : EtOAc : AcOH 9 : 1 : 0.01); m.p. 146.1 – 148.5 °C; $[\alpha]_D^{24}$ + 90.5° (*c* 0.57, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.86 (s, 1H), 6.21 (s, 1H), 2.69 (dd, *J* = 16.9, 5.0 Hz, 1H), 2.51 (s, 3H), 2.29 (dd, *J* = 16.9,

13.2 Hz, 1H), 2.08 (dt, *J* = 12.5, 3.1 Hz, 1H), 1.86 – 1.72 (m, 2H), 1.69 (dd, *J* = 13.1, 4.8 Hz, 1H), 1.66 – 1.58 (m, 1H), 1.55 (dd, *J* = 13.1, 5.0 Hz, 1H), 1.52 – 1.45 (m, 1H), 1.44 – 1.42 (m, 1H), 1.42 – 1.34 (m, 1H), 1.20 (s, 3H), 1.15 (dd, *J* = 13.4, 4.0 Hz, 1H), 1.03 (dd, *J* = 12.2, 2.2 Hz, 1H), 1.00 – 0.94 (m, 1H), 0.92 (s, 3H), 0.91 (s, 3H), 0.85 (s, 3H). ^{1}H NMR (500 MHz, CD_3OD) δ 6.11 (s, 1H), 2.65 (dd, *J* = 16.9, 5.0 Hz, 1H), 2.46 (s, 3H), 2.27 (dd, *J* = 16.7, 13.2 Hz, 1H), 2.05 (dt, *J* = 12.5, 3.2 Hz, 1H), 1.81 – 1.76 (m, 2H), 1.72 (dt, *J* = 13.7, 3.6 Hz, 1H), 1.69 – 1.61 (m, 1H), 1.52 (dd, *J* = 13.2, 5.2 Hz, 1H), 1.50 – 1.40 (m, 3H), 1.26 – 1.21 (m, 1H), 1.19 (s, 3H), 1.08 (dd, *J* = 12.2, 2.3 Hz, 1H), 1.05 – 0.98 (m, 1H), 0.96 (s, 3H), 0.92 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 163.9, 158.8, 141.3, 112.6, 108.1, 104.9, 78.4, 56.1, 51.5, 41.8, 40.8, 39.2, 37.0, 33.4, 33.2, 24.1, 21.6, 20.8, 19.7, 18.5, 16.7, 14.9); ^{13}C NMR (126 MHz, CD_3OD) δ 175.6, 164.5, 158.9, 141.7, 112.8, 108.8, 104.9, 79.0, 57.5, 53.2, 43.0, 42.1, 40.4, 38.1, 34.2, 33.9, 24.2, 22.0, 21.1, 20.8, 19.6, 17.7, 15.4; IR ν_{max} (neat) 2927, 1621, 1574, 1454, 1378, 1262, 1126 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{23}H_{33}O_4$ 373.2383; Found 373.2379; Anal. Calcd for $C_{23}H_{32}O_4$: C, 74.16; H, 8.66; Found: C, 74.22; H, 8.78.

7-(Allyloxy)-2,2,5-trimethyl-8-((2*E*,6*E*)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl)-4*H*-benzo[*d*][1,3]dioxin-4-one (28). Allyl bromide (0.65 mL, 7.50 mmol) was added with stirring to a suspension of K_2CO_3 (1.38 g, 10.0 mmol) and resorcylate **14** (2.06 g, 5.00 mmol) in Me_2CO (50 mL). The resulting suspension was heated to 60 °C with stirring for 18 h, when the mixture was concentrated and diluted with H_2O (50 mL) and CH_2Cl_2 (50 mL). The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : Et_2O 9 : 1) to provide allyl ether **28** (1.61 g, 3.56 mmol, 71%) as a pale yellow oil: R_f 0.33 (pentane : Et_2O 9 : 1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.41 (s, 1H), 6.04 (ddt, *J* = 17.3, 10.3, 5.1 Hz, 1H), 5.42 (dd, *J* = 17.3, 1.6 Hz, 1H), 5.30 (dd, *J* = 10.6, 1.4 Hz, 1H), 5.13 (tq, *J* = 7.3, 1.3 Hz, 1H), 5.07 (tdd, *J* = 6.9, 3.1, 1.4 Hz, 2H), 4.60 (dt, *J* = 5.1, 1.6 Hz, 2H), 3.29 (d, *J* = 7.3 Hz, 2H), 2.63 (s, 3H), 2.10 – 1.89 (m, 8H), 1.75 (s, 3H), 1.68 – 1.66 (m, 9H), 1.58 (s, 3H), 1.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 155.6, 142.5, 135.2, 134.9, 132.6, 131.2, 124.3, 124.1, 121.6, 117.6, 116.0, 109.3, 105.7, 104.7, 68.9, 39.74, 39.66, 26.7, 26.5, 25.73, 25.66, 22.5, 21.8, 17.6, 16.1, 16.0; IR ν_{max} (neat) 2969, 3925, 2856, 1729, 1606, 1575, 1376, 1278, 1207, 1169, 1115, 1046, 980, 908 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{29}H_{41}O_4$ 453.3005; Found 453.2983; Anal. Calcd for $C_{29}H_{40}O_4$: C, 76.95; H, 8.91; Found: C, 76.84; H, 8.87.

7-(Allyloxy)-8-((*R*,2*E*,6*E*)-10,11-dihydroxy-3,7,11-trimethyldodeca-2,6-dien-1-yl)-2,2,5-trimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (30). Allyl ether **28** (1.53 g, 3.38 mmol) was dissolved in ^{t}BuOH (17 mL) and H_2O (17 mL) and cooled to 0 °C. Ligand **29** (35 mg, 33.8 μmol), $MeSO_4NH_2$ (322 mg, 3.39 mmol), $K_3Fe(CN)_6$ (3.34 g, 10.1 mmol), K_2CO_3 (1.40 g, 10.1 mmol) and $K_2OsO_4{\cdot}2H_2O$ (6.3 mg, 17.1 μmol) were added sequentially with stirring at 0 °C. After 24 h, solid Na_2SO_3 (3.00 g) was added and the mixture was further stirred for 30 min. The reaction mixture was diluted with H_2O (25 mL) and EtOAc (25 mL), the two phases were separated, and the aqueous layer was extracted with EtOAc (3 × 25 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : EtOAc 4 : 1 to 1 : 1 to EtOAc : EtOH 4 : 1) to afford unreacted allyl ether **28** (400 mg, 0.88 mmol, 26%), tetraol (204 mg, 0.392 mmol, 12%), ligand **29** (33 mg, 32.3 μmol, 96% recovered) and diol **30** (956 mg, 1.96 mmol, 58%, 78% corrected for recovered allyl ether **28**, 88% *ee* as determined by Mosher ester analysis)[15] as a colourless oil: R_f 0.36 (pentane : EtOAc 1 : 1); $[\alpha]_D^{23}$ + 10.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.42 (s, 1H), 6.05 (ddt, *J* = 17.3, 10.4, 5.1 Hz, 1H), 5.42 (dd, *J* = 17.3, 1.6 Hz, 1H), 5.30 (dd, *J* = 10.6, 1.4 Hz, 1H), 5.19 – 5.10 (m, 2H), 4.61 (dt, *J* = 5.1, 1.6 Hz, 2H), 3.33 (dd, *J* = 10.5, 2.0 Hz, 1H), 3.29 (d, *J* = 7.4 Hz, 2H), 2.63 (s, 3H), 2.25 – 1.92 (m, 6H), 1.75 (s, 3H), 1.71 (s, 2H), 1.67 (s, 6H), 1.59 (s, 3H), 1.56 – 1.45 (m, 1H), 1.46 – 1.32 (m, 1H), 1.18 (s, 3H), 1.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.14, 161.08, 155.7, 142.7, 135.2, 135.1, 132.8, 125.1, 121.9, 117.9, 116.1, 109.5, 105.9, 104.9, 78.4, 73.1, 69.1, 39.9, 36.9, 29.8, 26.7, 26.6, 25.9 (2C), 23.4, 22.6, 21.9, 16.2, 16.0; IR ν_{max} (neat) 3443, 2931, 2972, 1729, 1606,1576, 1451, 1377, 1329, 1281, 1209, 1170, 1117 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{29}H_{43}O_6$ 487.3060; Found 487.3051; Anal. Calcd for $C_{29}H_{42}O_6$: C, 71.57; H, 8.70; Found: C, 71.69; H, 8.73.

7-(Allyloxy)-8-((2*E*,6*E*)-9-((*S*)-3,3-dimethyloxiran-2-yl)-3,7-dimethylnona-2,6-dien-1-yl)-2,2,5-trimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (31). Pyridine (2.20 mL, 27.3 mmol) and MsCl (0.28 mL, 3.62

mmol) were added sequentially with stirring to diol **30** in CH_2Cl_2 (20 mL). After 15 h, the mixture was diluted with Me_2CO (50 mL) and K_2CO_3 (20.0 g, 0.145 mol) was added and stirring continued for 24 h. H_2O (30 mL) was added and the two phases were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 40 mL) and the combined organic layers were dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : EtOAc 19 : 1 to 5 : 1) to give epoxide **31** (767 mg, 1.64 mmol, 90 %) as colorless oil: R_f 0.25 (pentane: EtOAc 19 : 1); $[\alpha]_D^{25}$ - 1.8° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.41 (s, 1H), 6.16 – 5.90 (m, 1H), 5.46 – 5.36 (m, 1H), 5.32 – 5.26 (m, 1H), 5.17 – 5.05 (m, 2H), 4.60 (d, *J* = 5.0 Hz, 2H), 3.28 (d, *J* = 7.3 Hz, 2H), 2.66 (t, *J* = 6.3 Hz, 1H), 2.62 (s, 3H), 2.17 – 1.91 (m, 6H), 1.74 (s, 3H), 1.66 (s, 6H), 1.57 (s, 3H), 1.67 – 1.48 (m, 2H), 1.28 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9 (2C), 155.5, 142.5, 135.0, 134.0, 132.6, 124.7, 121.7, 117.6, 115.9, 109.3, 105.7, 104.6, 68.9, 64.1, 58.2, 39.7, 36.2, 27.4, 26.5, 25.7 (2C), 24.9, 22.4, 21.8, 18.7, 16.1, 15.9; IR ν_{max} (neat) 2961, 2923, 1727, 1606, 1575, 1450, 1376, 1327, 1279, 1207, 1169, 1115 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{29}H_{41}O_5$ 469.2954; Found 469.2960.

8-((2*E*,6*E*)-9-((*S*)-3,3-Dimethyloxiran-2-yl)-3,7-dimethylnona-2,6-dien-1-yl)-7-hydroxy-2,2,5-trimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (33). Dimethylbarbituric acid (**32**) (217 mg, 1.39 mmol) and $Pd(PPh_3)_4$ (29 mg, 0.0251 mmol) were added sequentially with stirring to epoxide **31** (589 mg, 1.26 mmol) in CH_2Cl_2 (10 mL). After 1 h, the reaction mixture was concentrated and purified by chromatography (pentane : EtOAc 4 : 1) to afford epoxide **33** (491 mg, 1.15 mmol, 91%) as a colourless oil: R_f 0.30 (pentane : EtOAc 4 : 1); $[\alpha]_D^{26}$ + 13.8° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (s, 1H), 6.42 (s, 1H), 5.19 – 5.13 (m, 1H), 5.12 – 5.05 (m, 1H), 3.29 (d, *J* = 7.3 Hz, 2H), 2.77 (dd, *J* = 7.4, 4.9 Hz, 1H), 2.58 (s, 3H), 2.19 – 1.98 (m, 6H), 1.74 (s, 3H), 1.73 – 1.69 (m, 1H), 1.68 (s, 6H), 1.57 (s, 3H), 1.56 – 1.49 (m, 1H), 1.33 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 160.4, 155.9, 142.6, 136.8, 134.0, 124.5, 121.9, 113.5, 113.2, 105.0, 104.7, 64.6, 59.5, 39.3, 36.2, 27.0, 25.7, 25.7 (2C), 24.9, 22.0, 21.8, 18.7, 16.0 (2C); IR ν_{max} (neat) 3258, 2964, 2927, 1727, 1693, 1609, 1514, 1452, 1377, 1327, 1276, 1210, 1107 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{26}H_{37}O_5$ 429.2641; Found 429.2645.

(7a*R*,9a*R*,11*S*,13a*S*,13b*R*)-11-Hydroxy-2,2,5,7a,10,10,13a-heptamethyl-7a,8,9a,10,11,12,13,13a,13b,14-decahydro-4*H*,9*H*-benzo[*a*][1,3]dioxino[5,4-*j*]xanthen-4-one (34). $FeCl_3 \cdot 6H_2O$ (892 mg, 3.30 mmol) was added with stirring to epoxide **33** (470 mg, 1.10 mmol) in $MeNO_2$ (220 mL) and the resulting mixture was further stirred at 25 °C for 15 min. Saturated aqueous $NaHCO_3$ (150 mL) was added and the two phases were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL) and the combined organic layers were dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : EtOAc 3 : 1) to give meroterpenoid **34** (263 mg, 0.614 mmol, 56%, 92% *ee*, measured by chiral HPLC, Chiralpak® IE column, *n*-hexane : ^{i}PrOH 17 : 3, 5 mL/min, t_R = 18.9 [(-)-enantiomer], 25.8 [(+)-enantiomer] min) as a white foam: R_f 0.19 (pentane : EtOAc 3 : 1); $[\alpha]_D^{24}$ + 52.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.33 (s, 1H), 3.26 (dt, *J* = 11.0, 5.3 Hz, 1H), 2.56 (s, 3H), 2.56 – 2.49 (m, 1H), 2.25 (dd, *J* = 16.7, 13.1 Hz, 1H), 2.10 (dt, *J* = 12.5, 3.2 Hz, 1H), 1.86 – 1.76 (m, 2H), 1.72 (s, 3H), 1.68 (s, 3H), 1.73 – 1.60 (m, 3H), 1.52 (dd, *J* = 13.1, 5.0 Hz, 1H), 1.47 – 1.41 (m, 1H), 1.40 (d, *J* = 5.9 Hz, 1H), 1.19 (s, 3H), 1.12 (td, *J* = 13.0, 4.3 Hz, 1H), 1.03 (s, 3H), 1.02 – 0.98 (m, 1H), 0.92 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 158.6, 156.1, 142.1, 114.3, 108.0, 104.8, 104.0, 78.6, 78.1, 55.0, 51.1, 40.7, 38.8, 37.4, 36.7, 28.1, 27.1, 26.1, 25.5, 22.0, 20.7, 19.4, 16.5, 15.5, 15.0; IR ν_{max} (neat) 3440, 2930, 2867, 1713, 1616, 1574, 1452, 1388, 1286, 1207, 1126, 1043 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{26}H_{37}O_5$ 429.2641; Found 429.2646.

(3*S*,4a*R*,6a*R*,12a*R*,12b*S*)-3,11-Dihydroxy-4,4,6a,9,12b-pentamethyl-1,3,4,4a,5,6,6a,12,12a,12b-decahydro-2*H*-benzo[*a*]xanthene-10-carboxylic acid (35). H_2O (10 μL, 0.552 mmol) was added to a suspension of KO^{t}Bu (124 mg, 1.10 mmol) in Et_2O (1 mL) at 0 °C and stirred for 5 min. Meroterpenoid **34** (59 mg, 0.138 mmol) in Et_2O (1 mL) was added with stirring at 25 °C. After 3 h, ice was added until two layers were formed and the two phases were separated and diluted with Et_2O (2 mL). The pH was adjusted to ~ 1 with aqueous HCl (4 M). The two phases were separated and the aqueous layer was extracted with Et_2O (3 × 2 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : EtOAc : AcOH 3 : 1 : 0.01) to give the carboxylic acid **35** (37 mg, 0.0952 mmol, 69%) as a white

solid: R_f 0.14 (pentane : EtOAc : AcOH 4 : 1 : 0.01); m.p. 153 – 155 °C; $[\alpha]_D^{24}$ + 104.3° (*c* 0.3, CH_3OH); ^1H NMR (400 MHz, CD_3OD) δ 6.08 (s, 1H), 3.18 (dd, *J* = 11.3, 5.0 Hz, 1H), 2.61 (dd, *J* = 16.8, 5.0 Hz, 1H), 2.45 (s, 3H), 2.26 (dd, *J* = 16.7, 13.0 Hz, 1H), 2.03 (dt, *J* = 12.4, 3.2 Hz, 1H), 1.84 – 1.73 (m, 2H), 1.72 – 1.59 (m, 3H), 1.54 – 1.41 (m, 2H), 1.16 (s, 3H), 1.15 – 1.08 (m, 1H), 1.04 – 1.01 (m, 1H), 1.00 (s, 3H), 0.94 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 175.6, 164.4, 158.7, 141.7, 112.7, 108.6, 105.2, 79.4, 78.7, 56.5, 52.9, 42.1, 39.9, 38.8, 37.8, 28.7, 27.9, 24.2, 21.0, 20.5, 17.8, 16.2, 15.5; IR ν_{max} (neat) 3445, 2972, 2934, 2865, 1621, 1579, 1453, 1379, 1265, 1178, 1126, 1038 cm^{-1}; HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_{23}H_{31}O_5$ 387.2171; Found 387.2180.

(+)-Hongoquercin B [(3*S*,4a*R*,6a*R*,12a*R*,12b*S*)-3-Acetoxy-11-hydroxy-4,4,6a,9,12b-pentamethyl-1,3,4,4a,5,6,6a,12,12a,12b-decahydro-2*H*-benzo[*a*]xanthene-10-carboxylic acid (2)]. Ac_2O (63 μL, 0.666 mmol) was added with stirring to carboxylic acid **35** (37 mg, 0.0952 mmol) in pyridine (0.5 mL) at 25 °C. After 24 h, CH_2Cl_2 (2 mL) was added and the pH was adjusted to ~ 1 with aqueous HCl (4 M). The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 2 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated to give diacetate **36**. Crude diacetate **36** was dissolved in MeOH (2 mL) and H_2O (0.2 mL) and K_2CO_3 (20 mg, 0.143 mmol) was added at 25 °C. The resulting mixture was stirred for 5 h, when CH_2Cl_2 (2 mL) was added and the pH was adjusted to ~ 1 with aqueous HCl (4 M). The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 1 mL). The combined organic layers were dried (MgSO4), filtered and concentrated and chromatographed (pentane : EtOAc : AcOH 3 : 1 : 0.01) to give (+)-hongoquercin B (**2**) (27 mg, 0.0627 mmol, 66% over 2 steps from carboxylic acid **35**) as white solid: R_f 0.29 (pentane : EtOAc : AcOH 3 : 1 : 0.01); m.p. 155 – 157 °C; $[\alpha]_D^{30}$ + 91.0° (*c* 0.52, CH_3OH); ^1H NMR (400 MHz, $CDCl_3$) δ 11.85 (s, 1H), 6.21 (s, 1H), 4.52 (dd, *J* = 11.6, 4.7 Hz, 1H), 2.66 (dd, *J* = 16.8, 4.8 Hz, 1H), 2.52 (s, 3H), 2.30 (dd, *J* = 16.8, 13.1 Hz, 1H), 2.13 – 2.07 (m, 1H), 2.07 (s, 3H), 1.86 (dt, *J* = 13.3, 3.6 Hz, 1H), 1.81 – 1.60 (m, 4H), 1.53 (dd, *J* = 13.1, 5.0 Hz, 1H), 1.47 – 1.42 (m, 1H), 1.24 – 1.18 (m, 1H), 1.20 (s, 3H), 1.10 (dd, *J* = 12.1, 2.2 Hz, 1H), 0.96 (s, 3H), 0.91 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.9, 171.0, 163.8, 158.6, 141.6, 112.6, 107.7, 102.7, 80.4, 78.0, 55.1, 51.3, 40.6, 37.7, 37.1, 36.6, 28.1, 24.1, 23.5, 21.3, 20.7, 19.3, 16.8, 16.7, 15.0; IR ν_{max} (neat) 3063, 2972, 2941, 1731, 1623, 1580, 1454, 1371, 1263, 1178, 1126, 1035 ,1007 cm^{-1}; HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_{25}H_{33}O_6$ 429.2277; Found 429.2284.

(*E*)-7-(*Tert*-butyldimethylsilyloxy)-8-(3,7-dimethylocta-2,6-dienyl)-2,2,5-trimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (37). NEt_3 (1.08 mL, 7.72 mmol) was added with stirring to resorcylate **24** (806 mg, 2.34 mmol) in CH_2Cl_2 (50 mL) at 25 °C, when $^tBuMe_2SiCl$ (1.16 g, 7.72 mmol) and DMAP (5.72 mg, 0.0468 mmol) were added. The resulting mixture was stirred for 2 h, when 10% aqueous citric acid (30 mL) and CH_2Cl_2 (20 mL) were added. The two phases were separated and the organic layer was washed with 10% citric acid solution (2 × 30 mL), H_2O (30 mL) and brine (30 mL). The organic layer was dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : EtOAc 19 : 1) to give silyl ether **37** (815 mg, 1.78 mmol, 76 %) as a colorless oil: R_f 0.59 (pentane : Et_2O 10 : 1); ^1H NMR (400 MHz, $CDCl_3$) δ 6.36 (s, 1H), 5.13 – 5.00 (m, 2H), 3.24 (d, *J* = 7.0 Hz, 2H), 2.58 (s, 3H), 2.07 – 1.99 (m, 2H), 1.98 – 1.90 (m, 2H), 1.73 (s, 3H), 1.65 (s, 6H), 1.63 (s, 3H), 1.55 (s, 3H), 1.01 (s, 9H), 0.28 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 158.9, 156.4, 141.7, 134.9, 131.3, 124.1, 121.8, 118.4, 116.1, 105.9, 104.6, 39.6, 26.5, 25.7 (2C), 25.6 (4C), 22.2, 22.1, 18.2, 17.6, 16.2, -4.1 (2C); IR ν_{max} (neat) 2930, 2859, 1733, 1606, 1569, 1292, 1209, 1169, 1044, 841, 782 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{27}H_{43}O_4Si$ 459.2931; Found 459.2938; Anal. Calcd for $C_{27}H_{42}O_4Si$: C, 70.70; H, 9.23; Found: C, 70.52; H, 9.10.

(*S*,*E*)-7-((*Tert*-butyldimethylsilyl)oxy)-8-(5-(3,3-dimethyloxiran-2-yl)-3-methylpent-2-en-1-yl)-2,2,5-trimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (39). Silyl ether **37** (334 mg, 0.75 mmol) and the chiral ketone **38** (58 mg, 0.225 mmol) were dissolved in CH_2Cl_2 (6 mL), CH_3CN (3 mL), EtOH (3 mL) and aqueous buffer (2 M K_2CO_3; 4 × 10^{-3} M EDTA; 6 mL) and cooled to 0 °C. H_2O_2 (0.42 mL) was added dropwise with stirring. After 15 h, Na_2SO_3 (200 mg) was added and the phases were separated. The aqueous layer was extracted with Et_2O (3 × 15 mL) and the combined organic layers were dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : EtOAc 10: 1) to afford epoxide **39** (244 mg, 0.514 mmol, 69%) as a colorless oil:

R_f 0.22 (pentane : EtOAc 19 : 1); $[\alpha]_D^{23}$ + 2.8° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 6.35 (s, 1H), 5.12 (tq, *J* = 7.1, 1.3 Hz, 1H), 3.24 (d, *J* = 7.0 Hz, 2H), 2.65 (t, *J* = 6.2 Hz, 1H), 2.58 (s, 3H), 2.20 – 1.98 (m, 2H), 1.74 (s, 3H), 1.65 (s, 6H), 1.61 – 1.53 (m, 2H), 1.24 (s, 3H), 1.21 (s, 3H), 1.00 (s, 9H), 0.28 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 158.9, 156.3, 141.9, 134.1, 122.5, 118.1, 116.1, 105.9, 104.6, 64.0, 58.2, 36.2, 27.3, 25.8 (2C), 25.6 (3C), 24.8, 22.2, 22.1, 18.6, 18.3, 16.2, -4.0 (2C); IR ν_{max} (neat) 2959, 2930, 2859, 1732, 1605, 1570, 1279, 842 cm^{-1}; HRMS (FTMS) *m/z*: $[M + H]^+$ Calcd for $C_{27}H_{43}O_5Si$ 475.2874; Found 475.2870; Anal. Calcd for $C_{27}H_{42}O_5Si$: C, 68.31; H, 8.92; Found: C, 68.21; H, 9.03.

(*S*,*E*)-8-(5-(3,3-Dimethyloxiran-2-yl)-3-methylpent-2-en-1-yl)-7-hydroxy-2,2,5-trimethyl-4*H*-benzo[*d*][1,3]dioxin-4-one (40). K_2CO_3 (2.33 g, 16.9 mmol) was added with stirring to epoxide **39** (160 mg, 0.337 mmol) in Me_2CO (20 mL) at 25 °C. After 2 h, CH_2Cl_2 (30 mL) and H_2O (50 mL) were added and the two phases were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic layers were dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : EtOAc 5 : 1) to give epoxide **40** (112 mg, 0.311 mmol, 92 %) as colorless oil: R_f 0.29 (pentane : EtOAc 5 : 1); $[\alpha]_D^{24}$ - 9.4° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 6.40 (s, 1H), 6.17 (s, 1H), 5.30 – 5.15 (m, 1H), 3.31 (dd, *J* = 7.0, 2.1 Hz, 2H), 2.69 (dd, *J* = 6.8, 5.6 Hz, 1H), 2.58 (s, 3H), 2.26 – 2.07 (m, 2H), 1.80 (s, 3H), 1.68 (s, 6H), 1.69 – 1.55 (m, 2H), 1.28 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 159.8, 156.0, 142.8, 136.8, 121.7, 113.6, 113.0, 105.4, 104.8, 64.2, 58.6, 36.5, 27.2, 25.8, 25.7, 24.8, 22.0, 21.8, 18.7, 16.2; IR ν_{max} (neat) 3235, 2928, 1727, 1696, 1609, 1277 cm^{-1}; HRMS (FTMS) *m/z*: $[M + H]^+$ Calcd for $C_{21}H_{29}O_5$ 361.2010; Found 361.2016.

(7a*S*,10*S*,11a*S*)-10-Hydroxy-2,2,5,7a,11,11-hexamethyl-7a,8,10,11,11a,12-hexahydro-4*H*,9*H*-[1,3]dioxino[4,5-*a*]xanthen-4-one (41). BF_3OEt_2 (0.2 mL, 0.139 mmol) was added with stirring to epoxide **40** (110 mg, 0.305 mmol) in CH_2Cl_2 (30 mL) at -78 °C. After 5 min, Et_3N (5 mL) and H_2O (20 mL) were added, the mixture was allowed to warm up to 25 °C and the two phases were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic layers were dried ($MgSO_4$), filtered, concentrated and purified by chromatography (pentane : EtOAc 5 : 2) to give the meroterpenoid **41** (85 mg, 0.236 mmol, 77 %, 84% *ee*, measured by chiral HPLC, Chiralpak® IE column, *n*-hexane : ^{i}PrOH 9 : 1, 5 mL/min, t_R = 22.0 [(-)-enantiomer], 26.6 [(+)-enantiomer] min) as white foam: R_f 0.29 (pentane : EtOAc 5 : 2); $[\alpha]_D^{24}$ - 71.0° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 6.33 (s, 1H), 3.41 (dd, *J* = 11.4, 4.2 Hz, 1H), 2.63 (dd, *J* = 16.8, 4.9 Hz, 1H), 2.56 (s, 3H), 2.31 (dd, *J* = 16.9, 13.2 Hz, 1H), 2.00 (dt, *J* = 12.5, 3.3 Hz, 1H), 1.91 – 1.81 (m, 1H), 1.78 – 1.74 (m, 1H), 1.73 (s, 3H), 1.69 (s, 3H), 1.64 – 1.52 (m, 2H), 1.20 (s, 3H), 1.12 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 158.6, 156.0, 142.2, 114.3, 107.9, 104.8, 104.1, 77.8, 77.6, 46.1, 38.5, 37.4, 28.1, 27.3, 26.1, 25.4, 21.9, 19.8, 17.2, 14.3; IR ν_{max} (neat) 3433, 2942, 1708, 1617, 1573, 1287, 1128 cm^{-1}; HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_{21}H_{27}O_5$ 359.1858; Found 359.1853; Anal. Calcd for $C_{21}H_{28}O_5$: C, 69.98; H, 7.83; Found: C, 69.86; H, 7.94.

General procedure for BDSB (46) induced halocyclization. BDSB (**46**) (604 mg, 1.10 mmol) was added with stirring to resorcylate **24** or **14** (1.00 mmol) in $MeNO_2$ (50 mL) at -25 °C. After 10 min, saturated aqueous $NaHCO_3$ (15 mL) and aqueous Na_2SO_3 (0.5 M; 5 mL) were added and stirring was continued for 15 min. The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : Et_2O 9 : 1) to give the bromo-meroterpenoid **42** or **44**.

10-Bromo-2,2,5,7a,11,11-hexamethyl-7a,8,10,11,11a,12-hexahydro-4*H*,9*H*-[1,3]dioxino[4,5-*a*]xanthen-4-one (42). Bromide **42** (272 mg, 0.642 mmol, 64%), prepared from resorcylate **24** (344 mg, 1.00 mmol), was obtained as a white solid: R_f 0.29 (pentane : Et_2O 9 : 1); m.p. 225.3 – 225.7 °C; ^1H NMR (400 MHz, $(CD_3)_2CO$) δ 6.36 (s, 1H), 4.26 (dd, *J* = 11.8, 4.8 Hz, 1H), 2.80 – 2.77 (m, 1H), 2.52 (s, 3H), 2.50 – 2.43 (m, 1H), 2.30 – 2.13 (m, 2H), 2.00 (dt, *J* = 13.0, 3.5 Hz, 1H), 1.90 – 1.79 (m, 2H), 1.70 (s, 3H), 1.67 (s, 3H), 1.27 (s, 3H), 1.19 (s, 3H), 1.06 (s, 3H); ^{13}C NMR (101 MHz, $(CD_3)_2CO$) δ 160.7, 159.1, 157.0, 142.6, 115.1, 109.3, 105.8, 105.4, 78.2, 66.9, 47.9, 41.0, 40.1, 32.3, 29.9, 26.3, 25.6, 22.1, 20.2, 19.5, 17.4; IR ν_{max} (neat) 2975, 2924, 2865, 1715, 1616, 1575, 1380, 1286, 1128, 1044 cm^{-1}; HRMS (EI) *m/z*: $[M]^{\cdot+}$ Calcd for

$C_{21}H_{27}BrO_4$ 422.1093; Found 422.1110; Anal. Calcd for $C_{21}H_{27}BrO_4$: C, 59.58; H, 6.43; Found: C, 59.45; H, 6.57.

11-Bromo-2,2,5,7a,10,10,13a-heptamethyl-7a,8,9a,10,11,12,13,13a,13b,14-decahydro-4*H*,9*H*-benzo[*a*][1,3]dioxino[5,4-*j*]xanthen-4-one (44). Bromide **44** (219 mg, 0.446 mmol, 45%, 2 : 1 *dr*), prepared from resorcylate **14** (413 mg, 1.00 mmol), was obtained as a white solid containing a minor amount of a diastereoisomer: R_f 0.24 (Pentane/Et_2O 9:1); m.p. 234.0 – 237.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.33 (s, 1H), 4.00 (dd, *J* = 12.6, 4.7 Hz, 1H), 2.57 (s, 3H), 2.51 (dd, *J* = 16.8, 5.1 Hz, 1H), 2.37 – 2.13 (m, 3H), 2.13 – 2.07 (m, 1H), 1.91 – 1.84 (m, 1H), 1.84 – 1.78 (m, 1H), 1.72 (s, 3H), 1.71 – 1.69 (m, 1H), 1.69 (s, 3H), 1.59 – 1.46 (m, 2H), 1.20 (s, 3H), 1.20 – 1.11 (m, 2H), 1.12 (s, 3H), 0.99 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 158.5, 156.1, 142.2, 114.3, 107.8, 104.8, 104.1, 77.8, 68.4, 56.3, 51.1, 40.7, 40.5, 39.6, 37.0, 30.7, 30.6, 26.1, 25.5, 22.0, 21.1, 20.6, 18.3, 16.5, 14.9; IR ν_{max} (neat) 2949, 1718, 1613, 1575, 1376, 1288, 1131, 1042, 902, 844, 693 cm^{-1}; Anal. Calcd for $C_{26}H_{35}BrO_4$: C, 63.54; H, 7.18; Found: C, 63.49; H, 7.07.

General procedure for IDSI (47) induced halocyclization. IDSI (**47**) (884 mg, 1.10 mmol) was added with stirring to resorcylate **24** or **14** (1.00 mmol) in $MeNO_2$ (50 mL) at -25 °C. After 10 min, saturated aqueous $NaHCO_3$ (15 mL) and aqueous Na_2SO_3 (0.5 M; 5 mL) were added and stirring was continued for 15 min. The two phases were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : Et_2O 9 : 1) to give the iodo-meroterpenoid **43** or **45**.

10-Iodo-2,2,5,7a,11,11-hexamethyl-7a,8,10,11,11a,12-hexahydro-4*H*,9*H*-[1,3]dioxino[4,5-*a*]xanthen-4-one (43). Iodide **43** (415 mg, 0.882 mmol, 88%), prepared from resorcylate **24** (344 mg, 1.00 mmol), was obtained as a white solid: R_f 0.29 (pentane : Et_2O 9 : 1); m.p. 221.6 – 222.4 °C; ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 6.36 (s, 1H), 4.46 (dd, *J* = 11.9, 4.8 Hz, 1H), 2.82 (dd, *J* = 23.3, 6.7 Hz, 1H), 2.52 (s, 3H), 2.50 – 2.44 (m, 1H), 2.46 – 2.30 (m, 2H), 1.91 (dd, *J* = 13.2, 5.0 Hz, 1H), 1.87 – 1.82 (m, 2H), 1.70 (s, 3H), 1.67 (s, 3H), 1.28 (s, 3H), 1.16 (s, 3H), 1.09 (s, 3H); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 160.5, 158.9, 156.7, 142.4, 114.9, 109.3, 105.6, 105.2, 78.2, 50.1, 46.2, 42.5, 39.6, 34.9, 32.3, 26.1, 25.4, 21.9, 20.3, 20.0, 19.9; IR ν_{max} (neat) 2970, 1715, 1616, 1575, 1379, 1285, 1127, 1044, 902 cm^{-1}; HRMS (EI) *m/z*: $[M]^{\cdot+}$ Calcd for $C_{21}H_{27}IO_4$ 470.0954; Found 470.0947; Anal. Calcd for $C_{21}H_{27}IO_4$: C, 53.63; H, 5.79; Found: C, 53.55; H, 5.86.

11-Iodo-2,2,5,7a,10,10,13a-heptamethyl-7a,8,9a,10,11,12,13,13a,13b,14-decahydro-4*H*,9*H*-benzo[*a*][1,3]dioxino[5,4-*j*]xanthen-4-one (45). Iodide **45** (293 mg, 0.544 mmol, 54%, 2 : 1 *dr*), prepared from resorcylate **14** (413 mg, 1.00 mmol), was obtained as a white solid containing a minor diastereoisomer: R_f 0.24 (pentane : Et_2O 9 : 1); m.p. 189.5 – 192.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.33 (s, 1H), 4.24 (dd, *J* = 13.0, 3.2 Hz, 1H), 2.57 (s, 3H), 2.50 (dd, *J* = 16.4, 5.0 Hz, 1H), 2.46 – 2.29 (m, 2H), 2.24 (dd, *J* = 16.8, 13.1 Hz, 1H), 2.10 – 2.03 (m, 1H), 1.95 – 1.87 (m, 1H), 1.72 (s, 3H), 1.69 (s, 3H), 1.68 – 1.55 (m, 2H), 1.55 – 1.51 (m, 1H), 1.51 – 1.45 (m, 1H), 1.26 – 1.20 (m, 1H), 1.20 (s, 3H), 1.20 – 1.10 (m, 1H), 1.10 (s, 3H), 1.01 (s, 3H), 0.98 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 158.5, 156.1, 142.2, 114.3, 107.8, 104.8, 104.1, 77.3, 54.9, 52.9, 51.2, 42.2, 40.8, 39.3, 37.3, 33.6, 33.2, 26.1, 25.5, 22.2, 22.0, 21.1, 20.6, 16.5, 14.9; IR ν_{max} (neat) 2946, 1726, 1615, 1576, 1371, 1285, 1124, 1038, 902 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{26}H_{36}IO_4$ 539.1658; Found 539.1664.

2,2,5,7a,11,11-Hexamethyl-7a,8,10,11,11a,12-hexahydro-4*H*,9*H*-[1,3]dioxino[4,5-*a*]xanthen-4-one (48). $BF_3{\cdot}OEt_2$ (0.31 mL, 2.50 mmol) was added dropwise with stirring to resorcylate **24** (172 mg, 0.50 mmol) in CH_2Cl_2 (50 mL) at -78 °C. The resulting mixture was warmed to 25 °C and further stirred for 1.5 h, when saturated aqueous $NaHCO_3$ (25 mL) and H_2O (25 mL) were added and the phases were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 25 mL) and the combined organic layers were dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : Et_2O : 9 : 1) to provide meroterpenoid **48** (154 mg, 0.447 mmol, 89%, 3 : 1 *dr*) as a white solid containing a minor diastereoisomer. Recrystallization from *n*-hexane provided the pure *trans*-fused ring product: R_f 0.48 (pentane : EtOAc 19 : 1); m.p. 139.5 – 141.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.34 (s, 1H), 2.62 (dd, *J* = 16.8, 4.8 Hz, 1H), 2.57 (s, 3H), 2.22 (dd, *J* = 16.8, 13.3 Hz, 1H), 2.01 – 1.94 (m, 1H), 1.74 (s, 3H), 1.70 (s, 3H), 1.68 – 1.64 (m, 1H), 1.60 (dd, *J* = 13.4, 4.8 Hz, 1H), 1.60 – 1.55 (m, 2H), 1.54 – 1.47 (m, 1H), 1.37 – 1.28 (m, 1H), 1.21 (s, 3H), 1.03 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 160.9, 158.8, 156.0, 142.1, 114.4, 108.6, 104.8, 104.0, 78.7, 47.4, 41.4, 39.7, 33.5, 32.1, 26.2, 25.5, 22.0, 20.6, 19.8, 19.7, 17.3; IR ν_{max} (neat) 2969, 2901, 2921, 1720, 1618, 1576, 1390, 1286, 1043 cm^{-1}; HRMS (ESI) *m/z*: $[M]^{\cdot+}$ Calcd for $C_{21}H_{28}O_4$ 344.1988; Found 344.1990. Anal. Calcd for $C_{21}H_{28}O_4$: C, 73.32; H, 8.19; Found: C, 73.17; H, 8.22.

8-Hydroxy-1,1,4a,6-tetramethyl-2,3,4,4a,9,9a-hexahydro-1*H*-xanthene-7-carboxylic acid (49). H_2O (8 μL, 0.4 mmol) was added with stirring to a suspension of KO^{t}Bu (180 mg, 1.60 mmol) in Et_2O (3 mL) at 0 °C. After 5 min, meroterpenoid **48** (69 mg, 0.200 mmol) was added and the resulting mixture was further stirred at 25 °C for 2 h. The pH was adjusted to ~ 2 with aqueous HCl (1 M), the two phases were separated and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : EtOAc : AcOH 9 : 1 : 0.01) to give the carboxylic acid **49** (42 mg, 0.138 mmol, 69%) as a white solid: R_f 0.30 (pentane : EtOAc : AcOH 9 : 1 : 0.01); m.p. 176.7 – 178.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.84 (s, 1H), 11.17 (s, 1H), 6.22 (s, 1H), 2.77 (dd, *J* = 17.0, 4.8 Hz, 1H), 2.52 (s, 3H), 2.28 (dd, *J* = 16.9, 13.4 Hz, 1H), 2.01 – 1.94 (m, 1H), 1.72 – 1.64 (m, 1H), 1.64 – 1.55 (m, 3H), 1.55 – 1.45 (m, 1H), 1.40 – 1.27 (m, 1H), 1.22 (s, 3H), 1.04 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 163.7, 158.9, 141.4, 112.7, 108.4, 102.4, 78.7, 47.6, 41.5, 39.7, 33.6, 32.1, 24.1, 20.6, 19.8, 19.7, 17.6; IR ν_{max} (neat) 2694, 2919, 2865, 1619, 1578, 1454, 1268, 1151, 1100 cm^{-1}; HRMS (EI) *m/z*: $[M]^{\cdot+}$ Calcd for $C_{18}H_{24}O_4$ 304.1675; Found 304.1679; Anal. Calcd for $C_{18}H_{24}O_4$: C, 71.03; H, 7.95; Found: C, 71.17; H, 8.11.

1,1,4a,6-Tetramethyl-2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-8-ol (50). Aqueous KOH (5 M; 1 mL) was added with stirring to meroterpenoid **48** (69 mg, 0.200 mmol) in 1,4-dioxane (2 mL) and the resulting mixture was heated at 110 °C for 23 h. After cooling the reaction mixture to 25 °C, the pH was adjusted to ~ 2 with aqueous HCl (4 M). The two phases were separated and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : EtOAc 15 : 1) to give the phenol **50** (40 mg, 0.194 mmol, 97%) as white foam: R_f 0.33 (pentane : EtOAc 15 : 1); ^{1}H NMR (400 MHz, $(CD_3)_2CO$) δ 8.00 (s, 1H), 6.21 (s, 1H), 6.05 (s, 1H), 2.71 (dd, *J* = 16.7, 5.0 Hz, 1H), 2.26 (dd, *J* = 16.6, 13.5 Hz, 1H), 2.12 (s, 3H), 1.92 – 1.81 (m, 1H), 1.68 – 1.53 (m, 4H), 1.52 – 1.44 (m, 1H), 1.40 – 1.27 (m, 1H), 1.17 (s, 3H), 1.01 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (100 MHz, $(CD_3)_2CO$) δ 156.2, 155.0, 137.2, 109.7, 107.7, 107.6, 77.0, 48.8, 42.3, 40.8, 34.0, 21.3, 20.9, 20.4, 20.0, 18.6; IR ν_{max} (neat) 3398, 2935, 2866, 1627, 1587, 1516, 1457, 1101, 1063, 1040 cm^{-1}; HRMS (EI) *m/z*: $[M]^{\cdot+}$ Calcd for $C_{17}H_{24}O_2$ 260.1776; Found 260.1786.

7-(Hydroxymethyl)-1,1,4a,6-tetramethyl-2,3,4,4a,9,9a-hexahydro-1*H*-xanthen-8-ol (51). $LiAlH_4$ in THF (1 M; 0.8 mL, 0.800 mmol) was added with stirring to meroterpenoid **48** (69 mg, 0.200 mmol) in THF (4 mL) at 0 °C. After 1 h, H_2O (65 μL) and NaOH (1 M; 150 μL) were added dropwise sequentially and the mixture was further stirred for 30 min. Solid NH_4Cl (100 mg) was added and the solids were filtered and eluted with Et_2O (5 mL). The filtrate was concentrated and chromatographed (pentane : EtOAc 4 : 1) to afford diol **51** (55 mg, 0.189 mmol, 95%) as white foam: R_f 0.22 (pentane : EtOAc 9 : 1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 6.19 (s, 1H), 4.88 (s, 2H), 2.75 (dd, *J* = 16.6, 5.0 Hz, 1H), 2.37 – 2.27 (m, 1H), 2.17 (s, 3H), 1.99 – 1.90 (m, 1H), 1.69 – 1.54 (m, 4H), 1.52 – 1.40 (m, 1H), 1.38 – 1.25 (m, 1H), 1.20 (s, 3H), 1.02 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0, 153.4, 133.6, 113.6, 110.2, 109.0, 77.1, 60.8, 47.8, 41.6, 39.9, 33.5, 32.1, 20.6, 19.8, 19.6, 19.2, 17.7; IR ν_{max} (neat) 3344, 2934, 2865, 1627, 1583, 1102 cm^{-1}; HRMS (ESI) *m/z*: $[M - H]^-$ Calcd for $C_{18}H_{25}O_3$ 289.1804; Found 289.1807; Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02; Found: C, 74.59; H, 9.13.

8-Hydroxy-*N*-methoxy-*N*,1,1,4a,6-pentamethyl-2,3,4,4a,9,9a-hexahydro-1*H*-xanthene-7-carboxamide (52). MeNH(OMe)·HCl (59 mg, 0.605 mmol) was added dropwise with stirring to meroterpenoid **48** (69 mg, 0.200 mmol) in THF (4 mL) and cooled to 0 °C, followed by dropwise addition of ^{i}PrMgCl in THF (2 M; 0.6 mL, 1.20 mmol). The resulting mixture was stirred at 0 °C for 3 h, when the reaction was quenched with saturated NH_4Cl (2 mL) and the mixture was acidified to pH ~ 1 with aqueous HCl (1 M). The two phases were separated and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layers were dried ($MgSO_4$), filtered, concentrated and chromatographed (pentane : EtOAc 7 : 3) to

give the amide **52** (67 mg, 0.193 mmol, 96%) as a white solid: R_f 0.43 (pentane : EtOAc 7:3); m.p. 178.9 – 182.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.20 (s, 1H), 3.57 (s, 3H), 3.33 (s, 3H), 2.74 (dd, *J* = 16.7, 5.0 Hz, 1H), 2.28 (dd, *J* = 16.7, 13.4 Hz, 1H), 2.23 (s, 3H), 1.98 – 1.93 (m, 1H), 1.71 – 1.64 (m, 1H), 1.61 (dd, *J* = 13.2, 4.9 Hz, 1H), 1.59 – 1.54 (m, 2H), 1.54 – 1.45 (m, 1H), 1.37 – 1.24 (m, 1H), 1.20 (s, 3H), 1.02 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 155.5, 154.5, 135.3, 111.1, 110.7, 108.5, 77.7, 61.3, 47.7, 41.6, 39.9, 34.2, 33.5, 32.1, 20.6, 19.9, 19.8, 19.7, 17.8; IR ν_{max} (neat) 3110, 2933, 1616, 1578, 1456, 1389, 1120, 732 cm^{-1}; HRMS (ESI) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{30}NO_4$ 348.2175; Found 348.2188; Anal. Calcd for $C_{20}H_{29}NO_4$: C, 69.14; H, 8.41; N, 4.03; Found: C, 69.11; H, 8.49; N, 3.97.

ASSOCIATED CONTENT

^{1}H and ^{13}C NMR spectra for (+)-hongoquercin A (**1**), (+)-hongoquercin B (**2**), and compounds **14**, **20** – **21**, **24**, **27**, **28**, **30** – **31**, **33** – **35**, **37**, **39** – **41**, **42** – **45**, **48** – **52** and X-ray structural data for compounds **1**, **34**, **41** – **45** and **48**. This material is available free of charge via the Internet at http://pubs.acs.org.

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